The odd couple

Two distinct pathways in the visual cortex shadow each other from start to finish. Why?

The brain is often described as a parallel processor. This will have different connotations for different disciplines, and an anatomist will think of distinct neural pathways — but probably diverging from some common origin or converging on some common goal. In this context, 'parallel' means only the obverse of 'serial': the property of not meeting till infinity has been inconspicuous, at least until the recent description of a more authentically parallel pair of cerebral visual pathways [1]. The elements of this couple refuse to share the identical piece of cortex, yet they are never very far away from each other. Figuratively, they cannot live together and they cannot live apart. Remind you of anyone?

The origin of these two pathways is found within the superficial layers of the primary visual cortex of the brain (visual area V1). Unlike another 'two visual pathways' of popular neurology, which diverge towards the parietal and temporal lobes of the brain (more on these later), our pair ramify from V1 toward a number of separate destinations, always remaining firmly glued together. As yet, they have no very satisfactory terminology, but may be referred to according to the subunits of V1 from which they originate, the graphically named 'blobs' and 'interblobs'. These are modular structures, a few hundred microns in width, which are distinct by virtue of their metabolic machinery. Blobs contain more cytochrome oxidase, and appear as dark — well, blobs — in histochemical stains for this enzyme (Fig. 1). Interblobs are the paler-staining surrounding regions. For reasons that are still uncertain, the metabolic modules are also markers for the local differentiation of visual function, blobs being interested in spectral composition and low spatial frequencies, interblobs in edges and orientations [2–4].

Figure 1 summarizes the paired pathways that originate from blobs and interblobs. First stop is visual area V2, where the cytochrome oxidase stain reveals much larger structures in the form of stripes (Fig. 1). In exemplary cases, the dark stripes are alternately thick and thin in width, suggesting three sets of functionally distinct modules (which is borne out by other evidence). Blobs lead to the thin dark stripes and interblobs to the pale interstripes [2]. So far, so good. Both pathways then lead to area V4, but at this point, the cytochrome oxidase signal for functionally distinct modules vanishes; V4 and the other visual areas upstream of V2 all stain relatively homogeneously for this enzyme. No alternative marker is yet known, and if these areas do have a modular organisation, it can be diagnosed only indirectly. One way is by identifying patchy patterns of connectivity.

Neuroanatomists trace connections by injecting substances (such as peroxidase enzymes or dyes) that neurons absorb and transport up or down their axons. So the method reveals the neuronal connections of the specific piece of cortex in which tracer is deposited. The area involved can be made to be tiny, and certainly smaller than the dimensions of a hypothetical module, say 1–2 mm as a minimum width. When tracers are placed in area V4, the back-filled neurons in V2 tend to occur in one of two distinct patterns — in one they are largely restricted to the thin stripes, and in the other to the interstripes [5–7]. The clear implication is that V4 consists of at least two types of module, one acting as an extension of the blob–thin-stripe pathway and the other as an extension of the interblob–interstripe pathway. By using tracing dyes of different colours, it is possible to visualize both pathways simultaneously in the same cortical hemisphere, and also to examine the organization of the pathways across three or four levels of cortical hierarchy. The latter possibility follows from the fact that most, perhaps all, connections in the cerebral cortex are reciprocal. So it is not just the neurons providing an ascending input to V4 that are discovered, but also those that send feedback to V4 from a higher level. It is a fairly reliable guess that the latter will be sites that receive an ascending input from V4.

It is just this technique, of placing differently coloured dyes at nearby sites in V4, that has furnished the latest findings: in almost all the areas that can be shown to be connected to V4, the extensions of the interblob and blob pathways occupy contiguous, but largely non-overlapping, tracts of cortical territory [1]. Furthermore, the same trick can be used to chart the modules within V4. Paired placements of different dyes at nearby sites in the area immediately upstream from V4 (named TEO, for temporo-occipital, or PIT, for posterior infero-temporal) yield interlaced domains within V4 containing one or the other colour of back-filled cells [1]. The general conclusion is that the visual brain contains at least two genuinely parallel pathways. Unfortunately, this does not sound very newsworthy; indeed it is almost a cliché. Let us examine two of the alternative formulations of 'two visual pathways'.

Segregation of the visual pathway into two components occurs, indisputably, in the M (magnocellular) and P (parvocellular) layers of the lateral geniculate nucleus (LGN). What may be disputed is for how long the segregation is maintained. Nobody denies that both blobs and interblobs receive relays from the P cells of the LGN.

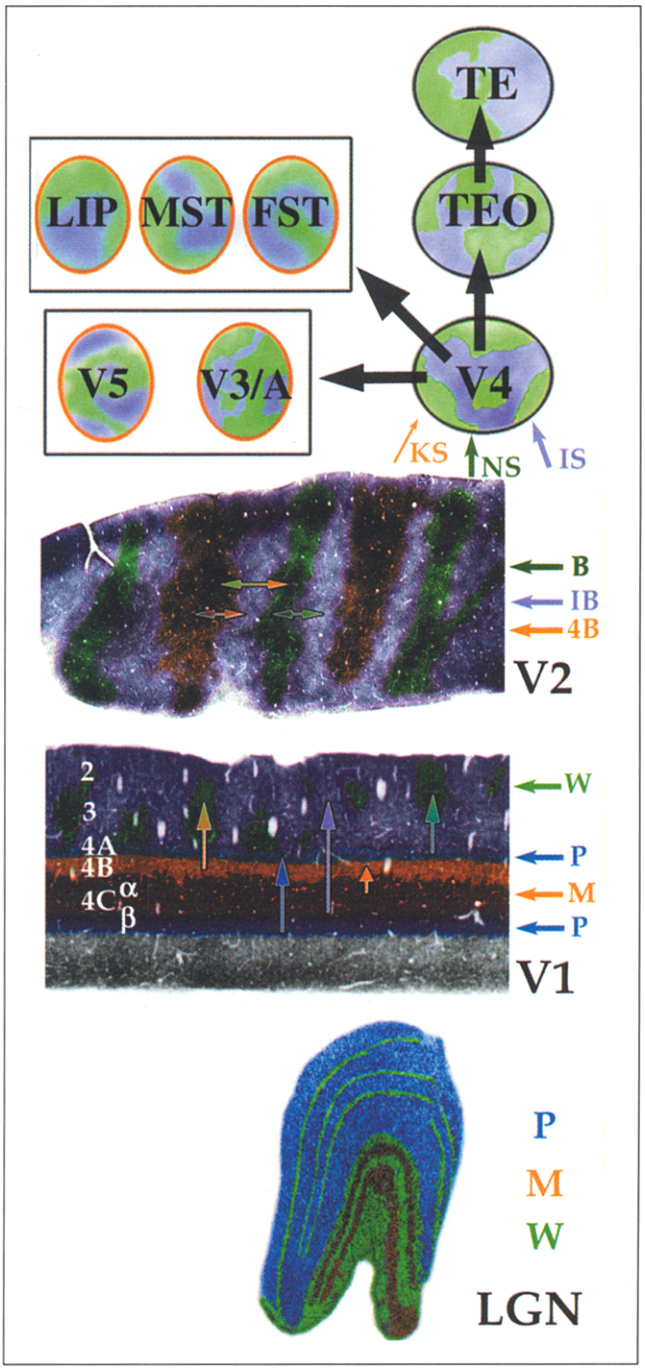

Fig. 1. The blob and interblob pathways, as seen from the perspective of V4. Colour-coded arrows show how the P, M and W layers of the lateral geniculate nucleus (LGN) feed into the layers 4Cα, 4Cβ, 4A and 3 of area V1 of the visual cortex. Note that M and P overlap at the boundary of 4Cα and 4Cβ. Internal relays effect further mixing, determining the composition of the output from layer 4B and from blobs (B) and interblobs (IB) to the thick stripes (KS), thin stripes (NS) and inter-stripes (IS) of V2. All three project to area V4, although the output from thick stripes is much the weakest. V4 projects to all the other areas shown, in which blob-stream and interblob-stream modules may be recognized (the shape of the green and lilac compartments is purely schematic). The distinctness of these modules is less emphatic in areas V5, MST, FST and LIP, all of which receive a more substantial M input from V1, V2 or V5 itself (denoted by an orange rim). Artwork by Grant Wray. Area name abbreviations: LIP, lateral intra-parietal; MST, medial superior temporal; FST, fundus superior temporal; TE, temporal; TEO temporo-occipital; V3/A, areas V3 and V3A.

Blobs contain wavelength-sensitive cells, a characteristic signature of the P system [2,3], whereas interblobs are the most responsive to high spatial frequencies [4], seemingly exploiting the fact that P cells are the most numerous class and have the smallest receptive fields, to fashion a fine-grained visual representation. There is no reason why subtly different local processing could not conjure up such different properties from a common P input and initiate the parallel outputs coursing through V2, V4 and beyond. Meanwhile, the M system can be seen to relay through a couple of layers of V1 directly to area V5, and to the same destination after a detour through the thick dark cytochrome stripes of V2 [8,9]; selectivity for the direction of moving stimuli is the hallmark of this system. Could it be that the P and M systems depart the LGN to diverge and deploy themselves in totally separate regions of the brain, with one handling fine form and colour, the other registering motion and three-dimensional space [10]? This heroic notion flowered briefly and artistically; sadly it is now rather firmly pressed between the pages of a steadily more stifling literature.

Several factors conspired in its demise. Most important, in the current context, is that both blobs and interblobs are now known to receive both P and M inputs. These can be traced anatomically through the maze of the intrinsic relays within V1 [11,12], or demonstrated physiologically. If the M layers of the LGN are inactivated, for example, visual responses in both blobs and interblobs are partially annulled [13]. The same technique of inactivating selected layers of the LGN has shown that M signals also reach visual area V4 [14]. There is an embarrassing richness in the number of routes they might take (see Fig. 1). Notwithstanding all this, a third system (best known as W) also gets in on the act. The W system is represented by very small neurons found within the gaps between the M and P layers of the LGN. Rather more numerous than previously appreciated, they also feed signals into the blobs [15], whose taste in visual input is evidently rather indiscriminate. Functionally speaking, W cells are something of a mixed bag, with large receptive fields and long latencies their only uniform characteristics [16].

There is therefore no such thing as a pure P pathway in the brain, because there is no part of the cortex, outside V1, where the P system maintains exclusive access. Does its erstwhile counterpart, the M system, fare any better? The answer is a qualified 'yes', because P input to areas such as V5 proves to be more negligible [17]. And this observation keys into another 'two pathway' dogma, one which holds that a dorsal pathway, stemming from V5, is largely separate and independent from a ventral pathway, fed mainly by V4 [18, 19]. This theory is a dichotomist's dream. The dorsal pathway is in the parietal lobe, is responsible for spatial vision, and depends on the M system; the ventral pathway is in the temporal lobe, is responsible for object vision, and feeds off the P system

[20–22] — or at least it was thought to, until recently; now we know it feeds off P, M and W.

The dorsal/ventral dichotomy is not an authentically 'parallel' conception, as the two empires are portrayed as parting company as soon as possible, and thereafter having as little to do with each other as possible. This sharply distinguishes it from the blob and interblob pathways which, in retaining their close association, happen to invade both the dorsal and the ventral sectors. Also, the dorsal/ventral dogma is curiously weak in its central tenet — the dichotomy. Space precludes a decent commentary, so an analogy must do. One might divide Africa into North and South, or North, South and Central, or any other way, or not at all. Only one piece of work (on the topological organization of connections) objectively supports a two-way split as the best description of visual cortex [23].

What can we learn from the anatomical structure of parallel pathways? One inference has always been clear — that morphological segregation is a clear index of specialized function. The layers of the LGN and V1, the cytochrome oxidase modules of V1 and V2, and areas V4 and V5 present examples across different dimensions and scales. What has become clear just recently is that the subdivisions at one stage will not necessarily relate in a one-to-one fashion with the subdivisions at the next. Thus, it was quite possible that the blob–thin-stripe and interblob–interstripe distinctions would begin to dissolve at the next stage in cortical processing. The results reviewed here suggest that they retain their identities — at least sufficiently to be recognizable one or two steps up the chain. But it would be folly to suggest that the cortex indulges in no further recombinations. Why, after all, should the blob and interblob pathways retain such a close association unless it were to facilitate some kind of interaction between them [9]? In retrospect, it is easy to envisage the blob and interblob streams attaining independence, immediately after their genesis, by being sent off to separate destinations outside V1. Instead, they both reappear in V2, neatly repackaged into parallel stripes and juxtaposed with the M system output from layer 4B. The range of intrinsic connections in V2 is just right to afford connections between all three types of stripe, and such connections have recently been documented [24]. In V4, the suspected size of the 'blob' and 'interblob' modules is slightly greater than in V2 [1], but so too is the lateral range of intrinsic connectivity [25–27]. There is no reason to suspect that this pattern, of intrinsic connectivity commensurate with local module size, should not be repeated in all cortical areas.

Finally then, the key question: what exactly do these pathways exchange? Their functional roles were initially expressed as serving colour and form perception [2,10]. Perhaps a more flexible formulation is to describe their jobs as determining the outlines of scenes, and objects, and filling in those outlines with surface features of texture, shading and colour (thus, the interblob pathway sketches boundaries, and the blob system paints them in) [28]. This is not a fanciful notion: there are well documented perceptual effects in which stabilized contours disappear, their contents replaced by the colours in their neighbourhood [29], or even by text, or dynamic 'twinkling' [30]. (This also relates to why the blind spot is invisible, even in monocular vision.) At the very least, contours extracted by the sketching system would need to be exported to the painting system. Yet the anatomy suggests a two-way exchange of signals, one that is repeated at several successive levels. We are very far from a theoretical, or even a physiological account of all that is happening. On the other hand it is possible to deduce the need for one or two exchanges between the subsystems, in respect of monocular and binocular stages, and in the interactions at different scales, or between foreground objects that occlude background objects. Why for instance are the 'Bs' of Figure 2 more visible when occluded than when fragmented? [28]

The idea of 'association cortex' is not new [31]. But some have seen the concepts of segregation and specialization of function as a contradictory viewpoint, and one to be

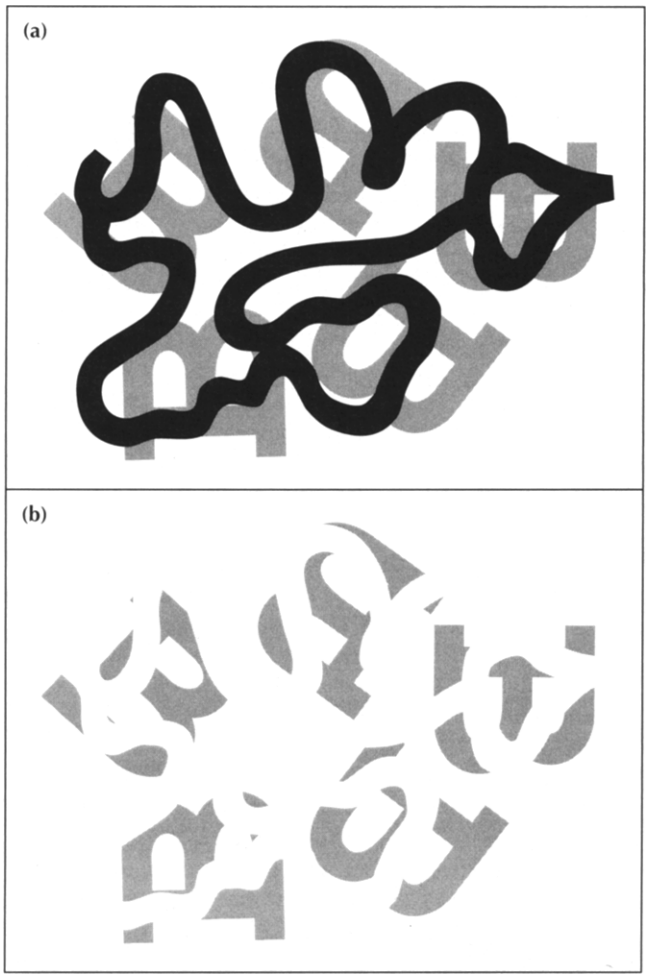

Fig. 2. The occluded Bs are normally recognized more rapidly than the fragmented Bs, although the visible parts are identical. See [28] for a theoretical exercise positing interactions between the blob and interblob streams that could account for this phenomenon. (Reproduced with permission from [32].)

decried. There is no contradiction as far as the cortex is concerned. Segregation is a tactic, an efficient means of composing an associable feature; association is the grand strategy. From this perspective the behaviour of the odd couple is not so odd after all: they have their own lives, but they'd be lost without each other.

References

1. DeYoe EA, Felleman DJ, Van Essen DC, McClendon E: **Multiple processing streams in occipitotemporal visual cortex**. *Nature* 1994, **371**:151–154.
2. Livingstone MS, Hubel DH: **Anatomy and physiology of a color system in the primate visual cortex**. *J Neurosci* 1984, **4**:309–356.
3. Tootell RBH, Silverman MS, Hamilton SL, DeValois RL, Switkes E: **Functional anatomy of macaque striate cortex. III. Color**.*J Neurosci* 1988, **8**:1569–1593.
4. Tootell RBH, Silverman MS, Hamilton SL, Switkes E, DeValois RL: **Functional anatomy of macaque striate cortex. V. Spatial frequency.** *J Neurosci* 1988, **8**:1610–1624.
5. Shipp S, Zeki S: **Segregation of pathways leading from area V2 to areas V4 and V5 of macaque monkey visual cortex**. *Nature* 1985, **315**:32–325.
6. Zeki S, Shipp S: **Modular connections between areas V2 and V4 of macaque monkey visual cortex**. *Eur J Neurosci* 1989, **1**:494–506.
7. Van Essen DC, Felleman DJ, DeYoe EA, Olavarria J, Knierim J: **Modular and hierarchical organization of extrastriate visual cortex in the macaque monkey.** *Cold Spring Harbor Symp Quant Biol* 1990, **55**:679–696.
8. Shipp S, Zeki S: **The organization of connections between areas V5 and V1 in macaque monkey visual cortex.** *Eur J Neurosci* 1989, **1**:309–332.
9. Shipp S, Zeki S: **The organization of connections between areas V5 and V2 in macaque monkey visual cortex.** *Eur J Neurosci* 1989, **1**:333–354.
10. Livingstone MS, Hubel DH: **Psychophysical evidence for separate channels for the perception of form, color, movement, and depth.** *J Neurosci* 1987, **7**:3416–3468.
11. Lachica EA, Beck P, Casagrande VA: **Parallel pathways in macaque monkey striate cortex: anatomically defined columns in layer III.** *Proc Natl Acad Sci USA* 1992, **89**:3566–3570.
12. Yoshioka T, Levitt JB, Lund JS: **Independence and merger of thalamocortical channels within macaque primary visual cortex: anatomy of interlaminar projections.** *Visual Neurosci* 1994, **11**:467–489.
13. Nealey TA, Maunsell JHR: **Magnocellular and parvocellular contributions to the responses of neurons in macaque striate cortex.** *J Neurosci* 1994, **14**:2069–2079.
14. Ferrera VP, Nealey TA, Maunsell JHR: **Responses in mącaque visual area V4 following inactivation of the parvocellular and magnocellular LGN pathways.** *J Neurosci* 1994, **14**:2080–2088.
15. Hendry SHC, Yoshioka T: **A neurochemically distinct third channel in the macaque dorsal lateral geniculate nucleus.** *Science* 1994, **264**:575–577.
16. Irvin GE, Norton TN, Sesma MA, Casagrande VA: **W-like responses of interlaminar cells in the lateral geniculate nucleus of a primate (*Galago crassicaudatus*).** *Brain Res* 1986 **362**:254–270.
17. Maunsell JHR, Nealey TA, DePriest DD: **Magnocellular and parvocellular contributions to responses in the middle temporal visual area (MT) of the macaque monkey.** *J Neurosci* 1990 **10**:3323–3334.
18. Ungerleider LG, Mishkin M: **Two cortical visual systems.** In *Analysis of Visual Behaviour.* Edited by Ingle DJ, Goodale MA, Mansfield RJW. Cambridge, Massachusetts: MIT Press; 1982:549–586.
19. Morel A, Bullier J: **Anatomical segregation of two cortical visual pathways.** *Visual Neurosci* 1990, **4**:555–578.
20. Mishkin M, Ungerleider LG, Macko KA: **Object vision and spatial vision: two cortical pathways.** *Trends Neurosci* 1983, **6**:414–417.
21. Maunsell JHR: **Physiological evidence for two visual subsystems.** In *Matters of Intelligence.* Edited by Vaina L. Dordrecht. Reidel; 1987:59-87.
22. Haxby JV, Grady CL, Horwitz B, Salerno J, Ungerleider LG, Mishkin M, Schapiro MB: **Dissociation of object and spatial visual processing pathways in human extrastriate cortex.** In *Functional Organisation of the Human Visual Cortex.* Edited by Gulyas B, Ottoson D, Roland P. Oxford, UK: Pergamon; 1993:329-340.
23. Young MP: **Objective analysis of the topological organization of the primate visual system.** *Nature* 1992 **358**:152–154.
24. Levitt JB, Yoshioka T, Lund JS: **Intrinsic cortical connections in macaque visual area V2: evidence for interaction between different functional streams.** *J Comp Neurol* 1994 **342**:551–570.
25. Yoshioka T, Levitt JB, Lund JS: **Intrinsic lattice connections of macaque monkey visual cortical area V4.** *J Neurosci* 1992 **12**:2785–2802.
26. Kritzer MF, Cowey A, Somogyi P: **Patterns of inter- and intralaminar GABAergic connections distinguish striate (V1) and extrastriate (V2, V4) visual cortices and their functionally specialized subdivisions in the rhesus monkey.** *J Neurosci* 1992, **12**:4545–4564.
27. Amir Y, Harel M, Malach R: **Cortical hierarchy reflected in the organization of intrinsic connections in macaque visual cortex.** *J Comp Neurol* 1993, **334**:19–46.
28. Grossberg S: **3-D vision and figure ground separation by visual cortex.** *Percept Psychophys* 1994 **55**:48–120.
29. Krauskopf J: **Effect of retinal image stabilization on the appearance of heterochromatic targets.** *J Opt Soc Am* 1963, **53**:741–744.
30. Ramachandran S, Gregory RL: **Perceptual filling in of artificially induced scotomas in human vision.** *Nature* 1991, **350**:699–702.
31. Flechsig P: **Developmental (myelogenetic) localisation of the cerebral cortex in the human subject.** *Lancet* 1901, **2**:1027–1029.
32. Nakayama K, Shimojo S, Silverman GH: **Stereoscopic depth: its relation to image segmentation, grouping, and the recognition of occluded objects.** *Perception* 1991, **18**:55–68.

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